

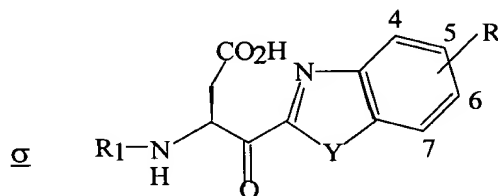
AMENDMENTS TO THE CLAIMS

Please add claims 135-141 as indicated below. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-101 (Canceled).

102. (Original) A compound represented by the formula:



wherein the ring is optionally substituted with one or more R groups, preferably 0, 1 or 2; and wherein:

R₁ is R₅-(A)_p-;

R₅ is selected from the group consisting of:

-H,

-Ar₁,

-CO-Ar₁,

-SO₂-Ar₁,

-R₉,

-CO-R₉,

Appl. No. 09/886,772
Amdt. Dated March 4, 2004

-CO-O-R₉,

-SO₂-R₉,

$$\begin{array}{c} \text{/Ar}_1 \\ \text{-CO-N} \\ \text{\R}_{10}, \end{array}$$

$$\begin{array}{c} \text{/Ar}_1 \\ \text{-SO}_2\text{-N} \\ \text{\R}_{10}, \end{array}$$

$$\begin{array}{c} \text{/R}_9 \\ \text{-CO-N} \\ \text{\R}_{10}, \end{array} \quad \text{and}$$

$$\begin{array}{c} \text{/R}_9 \\ \text{-SO}_2\text{-N} \\ \text{\R}_{10}; \end{array}$$

each A is independently selected from the group
consisting of any α -amino acid;

p is 0, 1, 2, 3 or 4;

Y is

-O-,
-S- or
-NH; and

R is:

-H,
-O-C₁₋₆ alkyl,
-NH(C₁₋₆ alkyl),
-N(C₁₋₆ alkyl)₂,
-S-C₁₋₆ alkyl,
-C₁₋₆ alkyl, or
-Q₂;

each R_9 is a C_{1-6} straight or branched alkyl group optionally singly or multiply substituted by -OH, -F, or =O and optionally substituted with one Ar_1 group;

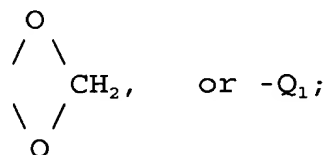
each R_{10} is independently selected from the group consisting of -H or a C_{1-6} straight or branched alkyl group;

each T_1 is independently selected from the group consisting of:

-CH=CH-,
-O-,
-S-,
-SO-,
-SO₂-,
-NR₁₀-,
-NR₁₀-CO-,
-CO-,
-O-CO-,
-CO-O-,
-CO-NR₁₀-,
-O-CO-NR₁₀-,
-NR₁₀-CO-O-,
-NR₁₀-CO-NR₁₀-,
-SO₂-NR₁₀-,
-NR₁₀-SO₂-, and
-NR₁₀-SO₂-NR₁₀-,

each Ar_1 is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, a cycloalkyl group which contains between 3 and 15 carbon atoms and between 1 and 3 rings, said cycloalkyl group being optionally benzofused, and a heterocycle group containing between 5 and 15 ring atoms

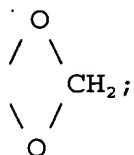
and between 1 and 3 rings, said heterocycle group containing at least one heteroatom group selected from -O-, -S-, -SO-, -SO₂-, =N-, and -NH-, said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -NH₂, -CO₂H, -Cl, -F, -Br, -I, -NO₂, -CN, =O, -OH, -perfluoro C₁₋₃ alkyl, O



each Q₁ is independently selected from the group consisting of:

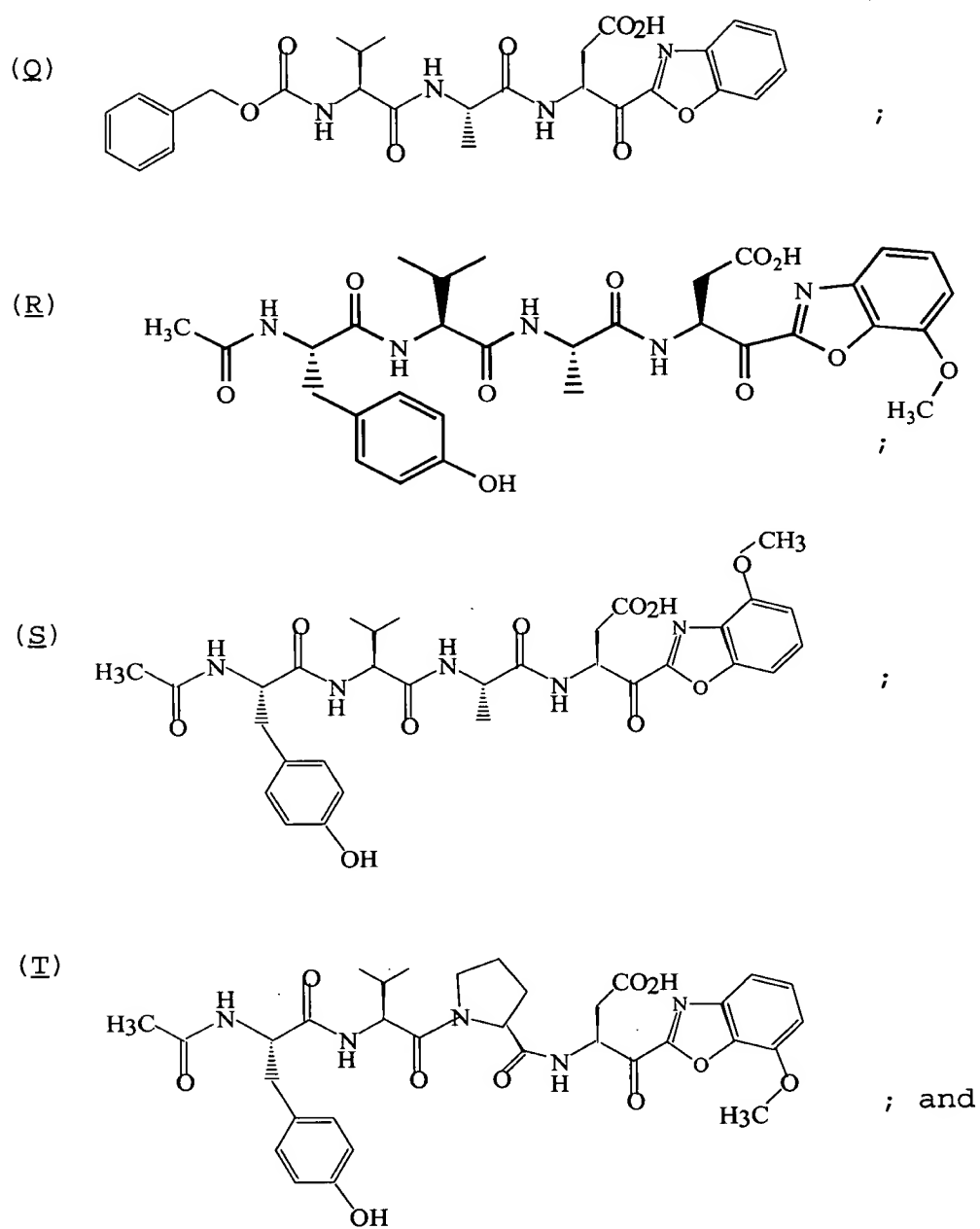
-Ar₁
-R₉,
-T₁-R₉, and
-(CH₂)_{1,2,3}-T₁-R₉;

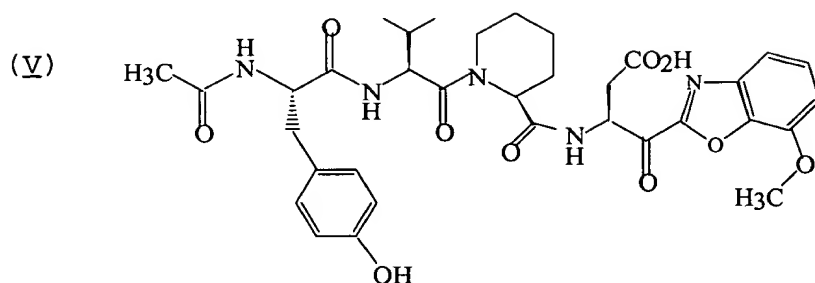
each Q₂ is independently selected from the group consisting of -OH, -NH₂, -CO₂H, -Cl, -F, -Br, -I, -NO₂, -CN, -CF₃, and



provided that when -Ar₁ is substituted with a Q₁ group which comprises one or more additional -Ar₁ groups, said additional -Ar₁ groups are not substituted with Q₁.

103. (Original) A compound according to claim 102 selected from the group consisting of:





104. (Original) A compound according to claim 102 wherein each A is independently selected from the group consisting of the α -amino acids:

alanine,
histidine,
lysine,
phenylalanine,
proline,
tyrosine,
valine,
leucine,
isoleucine,
glutamine,
methionine,
homoproline,
3-(2-thienyl) alanine, and
3-(3-thienyl) alanine.

105-124 (Canceled).

125. (Previously presented) A composition comprising a compound according to any one of claims 102-104 and a carrier.

126-128 (Canceled).

129. (Previously presented) The method for inhibiting IL-1 β secretion by LPS-stimulated human adherent mononuclear cells comprising administering to a mammal in need thereof a compound according to any one of claims 102-104 for a time and under conditions effective to inhibit interleukin-1 β converting enzyme.

130. (Previously presented) A method for inhibiting IL-1 β secretion by LPS-stimulated human peripheral blood monocytes comprising administering to a mammal in need thereof a compound according to any one of claims 102-104 for a time and under conditions effective to inhibit interleukin-1 β converting enzyme.

131. (Previously presented) A method of inhibiting interleukin-1 β converting enzyme comprising administering to a mammal in need thereof a compound according to any one of claims 102-104 for a time and under conditions effective to inhibit interleukin-1 β converting enzyme.

132. (Previously presented) The method according to claim 131, wherein the mammal is afflicted with a disease selected from the group consisting of septic shock,

septicemia, adult respiratory distress syndrome, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, insulin-dependent diabetes mellitus, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, multiple sclerosis, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, and primary lateral sclerosis.

133. (Previously presented) The method according to claim 131, wherein the mammal is afflicted with an infectious disease.

134. (Previously presented) A method of inhibiting interleukin-1 β converting enzyme comprising administering to a mammal in need of wound healing, a compound according to any one of claims 102-104 for a time and under conditions effective to inhibit interleukin-1 β converting enzyme.

135. (New) A method for preventing or treating inflammation, comprising contacting a cell population with an inhibiting effective amount of a reagent that suppresses the protease activity of at least one member of the interleukin-1 β -converting enzyme (ICE)/CED-3 family, thereby preventing or treating inflammation, wherein said inflammation is due to

an inflammatory disease, and wherein said inflammatory disease is selected from the group consisting of arthritis, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, and reperfusion injury.

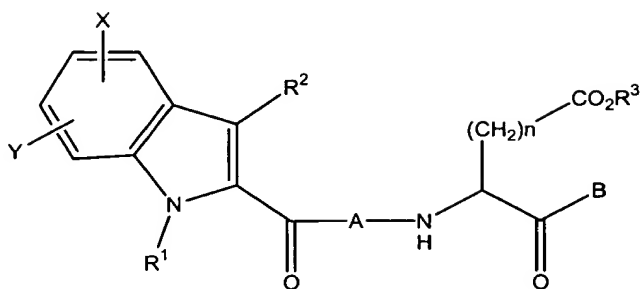
136. (New) The method of claim 135, wherein said inflammation is chronic inflammation.

137. (New) The method of claim 135, wherein said inflammation is acute inflammation.

138. (New) The method of claim 135, wherein the reagent suppresses the protease activity in an irreversible manner.

139. (New) The method of claim 135, wherein the reagent suppresses the protease activity in a reversible manner.

140. (New) The method of claim 135, wherein the reagent is a compound of formula 1:



FORMULA 1

wherein:

n is 1 or 2;

R¹ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or (CH₂)_mCO₂R⁴, wherein m=1-4, and R⁴ is as defined below;

R² is a hydrogen atom, chloro, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or (CH₂)_pCO₂R⁵, wherein p=0-4, and R⁵ is as defined below;

R³ is a hydrogen atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted)phenylalkyl;

R⁴ is a hydrogen atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted)phenylalkyl;

R⁵ is a hydrogen atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl,

(heteroaryl)alkyl, halomethyl, CH_2ZR^6 , $\text{CH}_2\text{OCO}(\text{aryl})$, $\text{CH}_2\text{OCO}(\text{heteroaryl})$; or $\text{CH}_2\text{OPO}(\text{R}_7)\text{R}_8$; where Z is an oxygen or a sulfur atom;

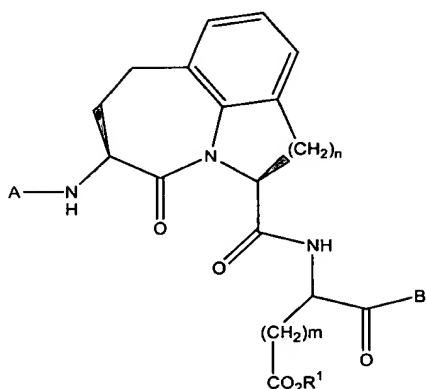
R^6 is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

R^7 and R^8 are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

141. (New) The method of claim 135, wherein the reagent is a compound of formula 3:



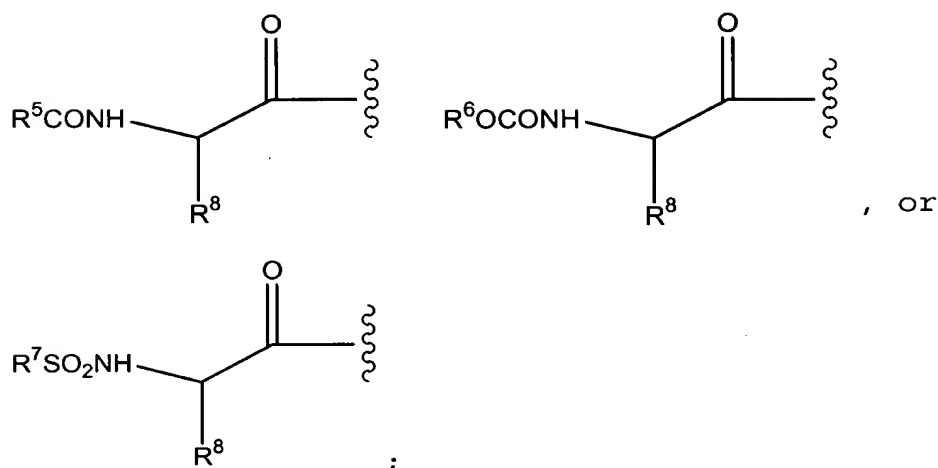
FORMULA 3

wherein:

n is 1 or 2;

m is 1 or 2;

A is R^2CO- , $R^3-O-CO-$, or R^4SO_2- , a group of the formula:



further wherein:

R^1 is a hydrogen atom, alkyl or phenylalkyl;

R^2 is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R³ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R⁴ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R⁵ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

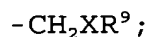
R⁶ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R⁷ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R⁸ is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:



wherein R⁹ is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:

Appl. No. 09/886,772
Amdt. Dated March 4, 2004

-CH₂-O-CO- (ARYL) ;

a group of the formula:

-CH₂-O-CO- (HETEROARYL) ;

a group of the formula:

-CH₂-O-PO(R¹⁰)R¹¹ wherein R¹⁰ and R¹¹ are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.